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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,383	09/08/2003	Yan Chang	104831-0002-103	9375

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EXAMINER	
MAIER, LEIGH C	

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1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/657,383	CHANG ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-12,15-23,25,26 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-12,15-23,25,26 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/15/08, 6/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-5, 7-12, 15-23, 25, 26 and 28 are pending. Any objection or rejection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. The rejections herein have been revised from the previous Office action. The arguments presented will be addressed insofar as they apply to the current rejections.

The declaration filed on June 30, 2008 under 37 CFR 1.131 has been considered but is ineffective to overcome the Klyosov et al (US 6,645,946) reference. The declaration is addressed below.

Claim Rejections - 35 USC § 103

Claims 1-4, 7, and 18-28 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Klyosov et al (US 6,645,946), as set forth in the previous Office action.

Klyosov '946 teaches the administration of galactomannan and 5-FU by injection to mice. See examples. It is noted that the mice in the examples do not actually have cancer. The reference also describes the structure of galactomannan. See paragraph bridging col 5-6. This structure appears to meet the criteria of carbohydrates that would bind to galectin-1 or galectin-3.

Although the reference does not exemplify administration to a patient having cancer, the reference specifically suggests the administration of the galactomannan/chemotherapeutic agent as a treatment for cancer. See col 2, lines 15-65. The reference teaches that the administration of

the galactomannan reduces side effects produced by toxic chemotherapeutic agents. See abstract. The reference further suggests a variety of modes of administration, including oral, and sequential administration of the galactomannan and chemotherapeutic agent. See col 3, lines 35-55, and col 4, lines 41-43 and reference claim 16.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer galactomannan with an oncolytic chemotherapeutic in order to reduce side effects produced by the chemotherapeutic agent with a reasonable expectation of success. As noted above, the reference is silent regarding "enhanced efficacy." However, the same patient population would be treated, regardless of whether the intent was to reduce side effects or enhance efficacy. Recognition of another advantage that would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. In the absence of unexpected results, it would be within the scope of the artisan to determine the optimum mode of administration and protocol regarding the relative timing of administration of the components through routine experimentation. It would be further obvious to combine the galactomannan/chemotherapeutic treatment with other common treatments such as radiation or surgical.

Applicant has submitted a declaration for the purpose of antedating Klyosov. The claim is drawn to the use of a generic carbohydrate which binds galectin and comprises a polymeric backbone. The reference teaches a species, and the declaration discloses another species. In order for a declaration disclosing a species to be sufficient to antedate the reference, the species completed prior to the reference date must provide an adequate basis for inferring that the invention has generic applicability. See MPEP 715.03 [R-2]. It is the opinion of the examiner

that the species provided would not provide one of ordinary skill the basis for envisioning a genus that would include galactomannan due to the great differences in structure of these substances. Applicant's species, modified citrus pectin, is an acidic heteropolymeric carbohydrate having irregular branching comprising a variety of monosaccharides. The affidavit does not disclose the molecular weight of the species, GBC590B, but the examiner assumes that it is approximately 10 kD, similar to the preferred embodiments as discussed in the specification. Galactomannan, on the other hand, is a neutral homopolymeric carbohydrate wherein the branching appears to be limited to galactose. The molecular weight of the preferred embodiments of Klyosov are much greater.

Claims 1-5, 7-9, 15-17, 20-23, 25, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (Anti-Cancer Drug Design, 1999) and Nangia-Makker et al (Am. J. Pathol., 2000).

Green teaches that glycoamines enhance the efficacy of taxol as an apoptotic agent in an *in vitro* system. See page 160. These glycoamines are antimetastatic agents whose activity is derived from their ability to bind β–galactoside-specific lectins (galectins). See page 159 at the 1st full paragraph. The reference does not teach a galectin-binding carbohydrate comprising a polymeric carbohydrate.

Nangia-Makker teaches that galectin-3 play an essential role in tumor growth and metastasis. Furthermore, endothelial cell morphogenesis—necessary for angiogenesis—is neutralized by specific sugars. See abstract. This neutralization is due to the binding of these sugars to galectin. One binding entity exemplified is modified citrus pectin. See page 903 and

page 907, 1st full paragraph. This agent completely inhibits cell motility and organization in capillary tube formation. In discussing this reference, Applicant admits that it teaches "[t]he materials of the present invention have been demonstrated to interact with galectins and inhibit angiogenesis." See specification at page 11, lines 15-20.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Green by the substitution of another agent, such as modified citrus pectin, demonstrated to have ability to bind galectin and interfere with processes necessary for tumor progression with a reasonable expectation of success. Green had taught the combination of a galactin-binding carbohydrate product increases the efficacy of a chemotherapeutic agent in the treatment of cancer, and Nangia-Makker had taught that modified citrus pectin binds galectin and inhibits metastasis and angiogenesis, important in treating cancer. It would be within the scope of the artisan to optimize the timing of the administration of the two agents through routine experimentation.

Applicant's arguments filed June 30, 2008 have been fully considered but they are not persuasive.

Applicant argues that Green provides no teaching that a carbohydrate comprising a polymeric backbone and binds to a galectin would be successful in the disclosed method. The examiner agrees that reference does not teach a galectin-binding carbohydrate comprising a polymeric carbohydrate. This was noted in the previous action. However, it teaches that the basis for the activity of disclosed agent, glycoamines, is the ability to bind to galectins.

Applicant further argues that Nangia-Makker does not teach enhancing the efficacy of a chemotherapeutic agent. However, one cannot show nonobviousness by attacking references

individually where the rejections are based on combinations of references. As discussed previously, it is Green that provides the suggestion to combine a galectin-binding substance with a chemotherapeutic agent. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The examiner maintains that one of ordinary skill would reasonably expect another agent, such as modified citrus pectin, having been disclosed as binding to galactins and having the ability to inhibit angiogenesis, would be useful for the treatment of cancer in combination with other therapeutic agents for their combined effect.

In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (Anti-Cancer Drug Design, 1999) and Nangia-Makker et al (Am. J. Pathol., 2000) as applied to claims -5, 7-9, 15-17, 20-23, 25, 26 and 28 above, and further in view of Raz et al (US 5,834,442).

Green and Nangia-Makker teach as set forth above. The references are silent regarding particular routes of administration.

Raz teaches that oral and intravenous administration of modified citrus pectin in the treatment of cancer is known. See col 2, lines 4-33.

It would have been obvious to one having ordinary skill in the art to modify the method of Green as set forth above. It would be further within the scope of the artisan to select any routine route of administration, such as oral or intravenous. One of ordinary skill would reasonably expect success in using either of these routes because they had been disclosed by Raz as being useful for administering modified citrus pectin.

Applicant's arguments filed June 30, 2008 have been fully considered but they are not persuasive. Applicant adds no additional argument not addressed above.

Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (Anti-Cancer Drug Design, 1999) and Nangia-Makker et al (Am. J. Pathol., 2000) as applied to claims -5, 7-9, 15-17, 20-23, 25, 26 and 28 above, and further in view of Platt et al (WO 97/34907), Ros et al, (Carbohyd. Res., 1996) and Renard et al, (Carbohyd. Res., 1995).

Platt teaches that modified citric pectin (MCP) with molecular weight of about 10 kD has utility in the treatment and prevention of metastatic cancer. See pages 1-3 and page 6, lines 2-6. The reference further suggests the use of other methodologies for the depolymerization of pectin.

Ros teaches the enzymatic hydrolysis of pectin. See pp 272-3.

Renard teaches the thermal hydrolysis of pectin. See pp 156-7, section 2.

It would have been obvious to one having ordinary skill in the art to modify the method of Green as set forth above. It would have been further obvious to one having ordinary skill in the art at the time the invention was made to use a pectin depolymerized by any known method,

such as enzymatic or thermal hydrolysis, known in the art to depolymerize pectin to arrive at the MCP having anti-metastatic activity for use in the method made obvious, as set forth above. Platt had taught the general physical requirements and suggested the use of other methods. Therefore it would be within the scope of the artisan to use the method taught by Ros to prepare an appropriate product through routine experimentation with a reasonable expectation of success.

Applicant's arguments filed June 30, 2008 have been fully considered but they are not persuasive. Applicant adds no additional argument not addressed above.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

/Leigh C. Maier/
Primary Examiner, Art Unit 1623
October 30, 2008